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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/279,275	07/22/1994	HOWARD L. WEINER	101016104US1	7626

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EXAMINER
EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
1644	78

DATE MAILED: 03/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
08/279,275	Weiner et al.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 13, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *29-41* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *29-41* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Dr. Gerald R. Ewoldt, Group Art Unit 1644.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/13/01 has been entered.

3. Note that new Claims 27-39 in the amendment submitted 11/13/01 have been renumbered 29-41 in accordance with 37 C.F.R. Rule 1.126 because the unentered amendment submitted 5/29/01 contained two new claims numbered 27 and 28. While Claims 27 and 28 of the 5/29/01 amendment have not been entered into the application, the claim numbers may not be reused.

4. Claims 29-41 are pending and being acted upon.

5. The disclosure is objected to because of the following informality, the instant application, filed 7/22/94, claims priority to U.S. Application Nos. 07/460,852 and 07/065,734. The first line of the specification must be updated to indicate the status of the priority applications.

6. New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

Corrections other than Informalities Noted by Draftsperson on form PTO-948. All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections. Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application.

7. In view of Applicant's amendment, filed 11/13/01, all previous rejections have been withdrawn.

8. The following are new grounds for rejection.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 29-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for,

a method for the treatment of myelin basic protein (MBP) induced experimental allergic encephalomyelitis (EAE) in Lewis rats, and a method for the treatment of adjuvant induced arthritis (AA) in Lewis rats,

does not reasonably provide enablement for,

a method for the treatment of a T cell-mediated or T cell-dependent autoimmune disease by suppressing an autoimmune response associated with said disease in a human suffering from said autoimmune disease, said method comprising orally or enterally administering to said human at least one antigen in an amount effective to suppress said autoimmune response, said antigen selected from the group consisting of autoantigens specific for said autoimmune disease, said suppression comprising elicitation of suppressor T cells specific to said administered antigen, or

a method of treating a T cell-mediated or T cell-dependent autoimmune disease by suppressing an autoimmune response associated with said disease in a human suffering from said autoimmune disease, said method comprising orally or enterally administering to said human at least one antigen in an amount effective to suppress said autoimmune response said antigen selected from the group consisting of autoantigens specific for said autoimmune disease.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including the breadth of the claims, the level of predictability of the art, the amount of direction provided by the specification, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

In the instant case, the specification discloses that the invention as broadly claimed would encompass a method of treatment for conditions ranging from multiple sclerosis (MS) to poison ivy. Note that contact dermatitis caused by poison ivy can not even properly be considered an autoimmune disease given the definition of autoantigen disclosed in the specification ("a response to substance normally found within an animal that, in an abnormal situation, is no longer recognized as part of the animal itself") as contact dermatitis caused by poison ivy is a response to a modified protein. Thus, the method of the instant claims must be considered to encompass a diverse collection of conditions comprising unrelated pathologies and etiologies. Further note that Claims 34, 36, and 37 recite a method of treating *any* autoimmune disease with MBP or bovine myelin basic protein (bMBP), a method which must be considered highly unpredictable.

Regarding the level of predictability of the art, it is well recognized that processes involving physiological activity, are generally considered unpredictable (see MPEP 2164.03). In particular, processes involving antigen specific treatments for autoimmune conditions must be considered highly unpredictable as essentially no such treatments were known as of the effective filing date of the instant application. Given the breadth of the instant claims and the unpredictability of the art, significant direction or guidance would be required to enable the instant invention. As set forth in MPEP 2164.03 "The "amount of guidance or direction" refers to that information in the application, as

originally filed, that teaches exactly how to make or use the invention." It is the Examiner's position that the instant application provides insufficient teachings regarding exactly how to use the claimed invention. The working examples disclosed in the instant application teach the induction and treatment of two artificial animal models of human autoimmune diseases (EAE as a model for MS and adjuvant induced arthritis (AA) as a model for rheumatoid arthritis (RA)). While the method of the instant claims may have provided a successful treatment in both animal models, in both cases the analogous treatment for humans was a failure. See Marketletter (1999) which teaches that both the bMBP-derived drug Myloral® (for MS) and the collagen-derived drug Colloral® (for RA) failed to perform better than placebos in Phase III clinical trials. Thus, in two separate instances the method encompassed by the instant claims has been demonstrated to be nonfunctional. Given such teachings, the method of the instant claims must then be considered highly unpredictable. As the methods encompassed by the instant claims must be considered on a case-by-case basis, generic claims, such as Claims 29 and 35, cannot be considered enabled.

In re Wands, 858 F.2d at 731, 8 USPQ2d 1400 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In view of the quantity of experimentation necessary, the lack of sufficient working examples encompassing the entirety of the claimed method, the unpredictability of the art, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicant's arguments, filed 11/13/01, have been fully considered but have not been found convincing. Applicant argues that U.S. Patent Nos. 5,869,054, 5,869,093, 5858,968, and 5,961977 "are probative of enablement of the presently claimed invention." It is the Examiner's position, however, that the evidence of the issued patents is insufficient to overcome the teachings of a reference that the specific invention of the instant claims does not function as claimed. Applicant further argues that "The present inventors discovered first a probable mechanism that would be mobilized by oral administration of autoantigen (see present Example 4 and Example 6) and then confirmed this mechanism (see present Example 10). This discovery permitted them to extrapolate to many diseases." However, a careful review of the Examples discloses no discussion or disclosure of any "mechanism" by which the claimed invention might function. Applicant appears to be attempting to

extrapolate a "mechanism" from the data now, some 15 years after the effective filing date of the instant application, a "mechanism" not disclosed in Example 4, 6, or 10 of the specification. Note that Applicant's arguments regarding Example 4 appear not to be related to the Example 4 of the instant application which discloses a reduction of a probably irrelevant antibody response. Applicant further argues that the invention of the instant claims is an extension of the findings of Cohen et al. "that autoimmune diseases can be transferred from a diseased animal to a healthy animal by transfer of a specific set of T cells that mediate the disease." Said findings cannot however, overcome the demonstration that in at least two instances (Myloral® for MS and Colloral® for RA), the method of the instant claims does not work as claimed.

11. Claims 34 and 36-41 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) a method for the treatment of a T cell-mediated or T cell-dependent autoimmune disease comprising administering an autoantigen, wherein said autoantigen is MBP, (Claim 34),

B) a method of treating a T cell-mediated or T cell-dependent autoimmune disease comprising administering an autoantigen, wherein said autoantigen is MBP,(Claim 36),

C) a method of treating a T cell-mediated or T cell-dependent autoimmune disease comprising administering an autoantigen, wherein said autoantigen is bMBP,(Claim 37),

D) a method wherein said autoantigen is contained in tissue that is the site of attack in the autoimmune disease, (Claims 38-41).

Applicant's amendment, filed 11/13/01, asserts that support for Claim 34 can be found in original Claim 15, however said claim provides support only for a method of treating MS by administering MBP. Said claim does not provide support for treating any autoimmune disease by administering MBP. Likewise, Claims 36 and 37 have no support in the specification as filed. Applicant asserts that support for Claims 38-41 can be found in canceled Claims 23-26, respectively, however, said claims were

not part of the specification as filed and therefore cannot support the newly submitted claims.

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 34 and 36 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 9, 14, 19, and 24 of U.S. Patent No. 5,869,054. Although the conflicting claims are not identical, they are not patentable distinct from each other because the claims recite a method of treating MS in a human comprising administering to said human MBP.

14. Claim 34 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 2 of U.S. Patent No. 6,036,957. Although the conflicting claims are not identical, they are not patentable distinct from each other because the claims recite a method of treating MS in a human comprising administering to said human an MBP autoantigen.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner

by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
March 18, 2001

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TECHNOLOGY CENTER 1600